UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,949	01/07/2002	Kazuhiro Nakashima	0397-0438P	6273

2292 7590 10/06/2004

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,949	NAKASHIMA ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/8/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims Under Examination

1. Claims 1-14 are pending in the application. Claims 1-14 are under examination.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. However, formal drawings can be deferred until application is allowed by the examiner.

Information Disclosure Statement

3. The information disclosure statement filed 4/8/02 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered. Sinkai Etsuro et al., Principle of Measurement of PAMIA, Sysmex J. Vol. 20, No. 1, pp. 77-78 (1997), has not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear what structural and functional cooperative relationship exists between the sensitized insoluble carrier particles in step a) and the unagglutinated particles in step b). If Applicant intends for these two elements to be the same in form, consistency of terminology is suggested in order to obviate this rejection. Same analogous comment or problem applies to claim 2.

Claim 1 is ambiguous in reciting, "mixing a whole blood sample with sensitized insoluble particles ... to cause an immune agglutination reaction" in step a) because it is unclear what elements in the whole blood sample, i.e blood cells having cell surface antigen, soluble antigen or antibody present in serum or plasma, and the insoluble particles, i.e. antibody or antigen immobilized thereto, would cause an immune agglutination to take place. Please clarify.

Claim 1 is vague and indefinite because it is unclear what Applicant intends to encompass in reciting the term, "sensitized" in step a). Additionally, the term "sensitized" appears to be a subjective term that lacks a comparative basis for defining its metes and bounds.

Claim 1 in step a) is also vague and indefinite in reciting, "smaller" in relation to erythrocytic cells because erythrocytes encompass erythroblasts and nucleated red

cells which are differentially larger in sizes. Accordingly, the recitation of "smaller that erythrocytes" used in this context is confusing and renders the claim indefinite.

Claim 1 is vague and indefinite in reciting, "blood cells" in steps c) and d) especially with regard to intensity of the scattered light being measured because blood cells encompass all of leucocytes, erythrocytes, and thrombocytes or platelets, all of which differ in size and granulation depending on cellular maturity, and phenomena associated thereto such as platelet aggregation and rouleaux formation of erythrocytes. Accordingly, it is unclear how setting a 1) threshold value for distinguishing unagglutinated particles and agglutinated particles, and 2) threshold value for distinguishing agglutinated particles and blood cells (including clumped platelets) can be performed, with regard to the intensity of scattered light by these different cell types.

Claims 2-12 have improper antecedent basis problems in reciting, "An immunoassay according to claim ...".

In claims 2, line 2, "form" should be --from--.

Claim 2 is indefinite and confusing in reciting, "converting the degree of agglutination into the concentration of an antigen or antibody in the whole blood sample" because it is unclear how the concentration of *cell surface antigens* encompassed by the recited "antigen in the whole blood sample" is measured and calculated, based on steps c) and d) of claim 1 and step e) in the instant claim, so that the degree of agglutination can be converted into the concentration of a cell surface antigen.

Claim 2 lacks clear antecedent support in reciting, "calibration line produced beforehand". Alternatively, it is unclear Applicant intends to encompassed by "a calibration line produced beforehand".

Claim 3 lacks antecedent support in reciting, "the number of the blood cells". Further, it is unclear what Applicant intends to encompass in reciting, "the blood cells" since blood cells encompass all of erythrocytes in claim 1, step a), leucocytes, and thrombocytes. See also claims 5 and 7.

Claims 4 and 5 are ambiguous in reciting, "the concentration of the antigen or antibody in the whole blood" in relation to claim 2 from which they depend. Same analogous comments and problems regarding the recitation of "antigen or antibody" in claim 2, apply to claims 4 and 5.

Claim 11 is indefinite because it is unclear how "a counting immunoassay" relates to the claimed "immunoassay".

Claim 12 is confusing in reciting, "whole blood samples, among which a serum sample is involved" because it is unclear what Applicant intends to encompass in reciting the term, "involved" as used in the claim. How is a serum sample "involved" with whole blood samples. Please clarify.

Claim 13 is vague and indefinite. Same analogous comments and problems in claim 1 apply to claim 13.

Claim 13 is vague and indefinite because it is unclear what structural and functional cooperative relationship exists between the recitation of "light signal" in line 12 and the "scattered light generated" in line 10 in the instant claim.

Claim 14 has improper antecedent basis problems in reciting, "An immunoassay according to claim ...".

In claim 14, line 3, "form" should be --from--.

Claim 14 is vague and indefinite. Same analogous comments and problems in claim 2 apply to claim 14.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 2, and 9-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Moskowitz et al. (US 2001/0046685).

Moskowitz et al. disclose an immunoassay comprising mixing a whole blood sample with insoluble carrier particles (matrix) having antigen or antibody (fibrinogen or antibody to platelet cell surface glycoprotein receptor) immobilized thereto, subjecting the resulting immune agglutination reaction mixture including both agglutinated and unagglutinated particles) to irradiation with laser light in the infrared region, then

detecting scattered light generated therefrom. A control value is used in setting a base value (threshold value) for distinguishing unagglutinated particles from agglutinated particles and a standard calibrator is used to provide a standard curve for comparison with test results. The degree of agglutination is related to the concentration of antigen or antibody in the whole blood sample. The degree of agglutination is platelets is also determined and related to the number of platelets (blood cells) (see page 6, column 2 [0069] to page 7, column 2 [0071]) and column 8 [0080]). Extent of agglutination is measured nephelometrically (light scatter) (see page 8 [0079]). The insoluble carrier particles are at least about 0.1 um – 10 um (see page 3, column 1 [0035-0039]). Desirably, the immunoassay is performed at a temperature of at least 25 °C and in the range of 30 °C-40 °C and read at a time within 10 seconds to 5 minutes (see page 8, column 1 [0078] and column 2 [0087]). Confirmation of results has been confirmed by flow cytometry (see Figure 4 and page 10, column 1 [0123]).

6. Claims 13 and 14 are rejected under 35 U.S.C. 102 (b) as being anticipated by Kosako (US Patent 5,527,714).

Kosako discloses an immunoassay apparatus comprising flow cell having a mixing (agitating) part and dispensing mechanism for presenting a reaction mixture to the flow cell, a laser for irradiating particles through a flow cell, a detector (photo acceptance unit) for detecting scattered light, a signal processing means having a microcomputer for converting the light signal into an electrical signal for analysis and measurement of stored digital values and for setting threshold values for distinguishing

particle size distribution between agglutinated particles and unagglutinated particles. The detector is connected to an amplifier where electrical signal is converted to a digital message by an A/D converter (see column 3, lines 14-51, column 5, lines 1-18, and column 6, lines 1-15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-4 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kosako (US Patent 5,527,714) in view of Moskowitz et al. (US 2001/0046685).

Kosako discloses an immunoassay comprising mixing an analyte sample with insoluble carrier particles sensitized with antibody, agitating the reaction mixture,

subjecting the resulting immune agglutination reaction mixture including both agglutinated and unagglutinated particles to irradiation with laser, then nephelometrically detecting scattered light generated therefrom. The degree of agglutination is measured, and total particle size distribution curve is plotted including predetermined threshold values of unagglutinated particles, agglutinated particles, and spurious particles. The total resultant particles plotted in the distribution curve include agglutinated particles, unagglutinated particles, and other (spurious) particles wherein a first size distribution of the total particles and a second size distribution of spurious particles are determined and subtracted from the first distribution to produce a corrected size distribution of insoluble particles; hence, correcting for the concentration of analyte (antigen or antibody). Therefrom, the actual concentration of antigen or antibody is obtained (see column 3, lines 27-41 and claim 1).

Kosako differs from the instant invention in failing to disclose that the analyte sample is whole blood and the spurious particles are blood cells.

Moskowitz et al. has been discussed supra.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute whole blood as taught in the method of Moskowitz into the method of Kosako wherein agglutinated portion, unagglutinated portion, and spurious particles are taken into account for accuracy of nephelometric assay results because use of whole blood in the agglutination assay of Moskowitz has the advantage of less sample handling and the Kosako reference which appears to be generic in the

type of analyte mixture used provides significant improvement in assaying for analyte in a heterogeneous sample such as whole blood.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kosako (US Patent 5,527,714) in view of Moskowitz et al. (US 2001/0046685) as applied to claims 1-3 and 9-12 above, and further in view of Steel et al. (WO 98/20351).

Kosako and Moskowitz et al. have been discussed supra. Kosako and Moskowitz et al. differ from the instant invention in failing to teach that the scattered light is a forward scattered light.

Steel et al. provide that certain agglutination assays use optical flow particle analyzers that detect agglutination formation or the degree of non-agglutination by measuring forward scattered light and using particles having different sizes (see page 2, linrs 6-14).

One of ordinary skill in the art at the time the invention was made would have been motivated to measure forward scattered light as taught by Steel in the nephelometric assays taught by Kosako as modified by Moskowitz for measuring degrees of agglutination because Steel specifically taught that forward scattered light has the advantage of measuring different sizes of particles and aggregation formation in an assay mixture.

Prior Art

9. Claims 5-7 are clear of the prior art. Claims 5-7 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Maines et al. (US Patent 4,279,506) teach methods for counting particulate components in blood and measuring for MCV.

Coller (US Patent 5,854,005) discloses an assay for determining glycoprotein IIb/IIIa receptor blockade in whole blood.

Yamao et al. (US Patent 6,030,845) discloses agglutination assay for lysed whole blood.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
September 30, 2004

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
10/1/04